Remarks/Arguments:

Applicants respectfully request reconsideration of this application, as amended, and entry of this paper. Claims 4-6 and 8-13 were pending in the application. Without prejudice or disclaimer, claim 11 was amended and claim 13 was cancelled. Applicants reserve the right to prosecute any withdrawn or cancelled subject matter in a later filed divisional or continuation application.

1. Rejection of claims 4, 12, and 13 under 35 U.S.C. 112, first paragraph (Enablement and Written Description).

Claims 4, 12 and 13 were rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which its pertain, or with which it is most nearly connected, to make and use the invention. These claims were also rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the invention.

Though Applicants stated in its Response to the Office Action, mailed February 25, 2003, that it was in the process of making deposits of certain plasmids, Applicants now believe that such deposits are not necessary for the plasmids claimed in claims 4, 12 and 13 as the specification provides technical details sufficient to meet the enablement and written description requirements of 35 U.S.C. 112, first paragraph.

The rule is that a "[b]iological material need not be deposited, *inter alia*, if it is known and readily available to the public or can be made or isolated without undue experimentation." 37 CFR 1.802(a). Further, material may be incorporated by reference, *Ex parte Schwarze*, 151 USPQ 426 (Bd. App. 1966). An application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent, (2) a U.S. patent application publication, or (3) a pending U.S. application.

a. Claim 4, Plasmid JB-3120-2.

Applicants believe that the Instant Application meets the both enablement and written description requirements of 35 U.S.C. 112, first paragraph with respect to claim 4 claiming the plasmid JB-3120-2. At page 2, lines 14-17 of the Instant Application, the material of U.S. Patent No. 5,506,139 ('139 Patent) is incorporated by reference into the Instant Application. In the '139

Patent at column 12, line 10 through column 13, line 41 and Figures 1 and 2, the cloning and characterization (nucleic acid sequence and deduced amino acid sequence) of the *hin47* gene is taught. Column 13, line 61 through column 14, line 26 of the '139 Patent also teaches the generation of mutant *hin47* genes by site-directed mutagenesis, including the mutant, H91A *hin47*. These teachings are incorporated by reference into the Instant Application. Therefore, the rejection is improper and withdrawal of the rejection is respectfully requested.

b. Claim 12, Plasmid DS-2342-2-2.

Applicants believe that the Instant Application meets the enablement and written description requirements of 35 U.S.C. 112, first paragraph with respect to claim 12 claiming the plasmid DS-2342-2-2. At page 3, lines 15-20 of the Instant Application, the material of U.S. Patent No. 6,335,182 ('182 Patent) is incorporated by reference into the Instant Application. In the '182 Patent at column 18, line 15 through column 19, line 4 and Figures 4, 5A, 5B, 6 and 6A the construction of the plasmid BK-96-2-11 comprising the T7 promoter and *V38 hia* gene is taught. Column 20, line 15-34, together with Figure 10, of the '182 Patent teaches the expression of the *V38 hia gene*. These teachings are incorporated by reference into the Instant Application. BK-96-2-11 was deposited with ATCC on February 11, 1999 pursuant to the Budapest Treaty and has an accession number of 203771. Therefore, the rejection is improper and withdrawal of the rejection is respectfully requested.

c. Claim 13, Plasmid JB-3145-1.

In order to expedite prosecution, Applicants have canceled claim 13, so rejection of this claim under 35 U.S.C. 112, first paragraph for lack of enablement and written description is moot. In view of the above, Applicants respectfully request that the Examiner withdraw the enablement and written description rejections of claims 4, 12 and 13 under 35 U.S.C. 112, first paragraph.

2. Rejection of claims 5, 6 and 8 under 35 U.S.C. 103(a).

Claims 5, 6 and 8 stand rejected in a prior action (Office Action, mailed June 4, 2002) under 35 U.S.C. 103(a) as being unpatentable over Bass (Bass, S. et al., *J. Bacteriology*, 178:1154-61 (1996)), in view of the 1998 Article (Loosmore, S.M. et al., *Infection and Immunity*, 66(3): 899-906 (1998)) and Spaete (U.S. Patent No. 5,474,914 issued Richard Spate).

The Examiner alleged that Bass teaches Hin47 would be useful as a chaperone protein. The Examiner also alleges that the 1998 Article teaches recombinant vectors for production of

non-proteolytic Hin47 analogs made by mutation of the wild type Hin47 at amino acids, 91 (H91A), 121 (D121A) and 197 (S197A). Though these references in combination are alleged to teach that a non-proteolytic form of Hin47 may be used as a chaperone protein, the Examiner admits that they do not teach the co-expression of Hin47 with another protein. To supply what is not taught, the Examiner alleged that the Spaete teaches co-expression of two recombinant proteins, a chaperone protein and a second protein from a vector, provided that the chaperone is compatible with the second protein and secretion of the proteins is accomplished by including a leader sequence in the vector encoding the chaperone, the leader sequence generally being a signal peptide directing cell secretion. To combine the teaching of these references, the Examiner alleged that one of ordinary skill in the art would have known from the references above that Hin47 could be used in the disclosed vector and therefore the vector of claim 5 is obvious in light of the prior art.

Section 2142 of the MPEP states: "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985)".

Applicant has previously argued that the teaching of Bass was conjecture and would not be relied upon by one with oridinary skill in the art. In response, the Examiner now cites Spiess et al., *Cell*, 97:337-347 (April 1999) and Faccio et al., *J. Biol. Chem.*, 275(4): 2581-2588 (January 2000) in support of what Bass' alleged teachings. Applicants respectfully disagree that the addition of Spiess and Faccio strengthen the Examiner's allegation of obviousness as to the pending claims.

First, the teaching of Spiess and Faccio are made in reference only to the HtrA chaperone protein of *E. coli*. Faccio (page 2581, second column) refers to bacterial HtrA and cites Spiess, C. et al., *Cell*, 97: 339-347 (1999) which in turn at page its page 345 indicates that the HtrA chaperone protein studied was derived from the *HtrA* gene (referred to as the *DegP* gene) of *E. coli*. Thus, the teachings of Spiess and Faccio relate only to the chaperone protein, HtrA, derived from *E. coli*.

Instant claims 5,6 and 8 refer to Hin47 analogs derived from the *HtrA* gene of *Haemophilus*, with claim 5 being the independent claim from which claims 6 and 8 depend. Claim 5 is directed to an expresson vector comprising a nucleic acid molecule encoding the specified analogs of Hin47 which are derived *Haemophilus*. As *E. coli* is species of bacteria from the family *Enterobacteriaceae*, and *Haemophilus influenzae* is a species of bacteria from the family *Pasteurellales*, it would be expected that the amino acid sequences of HtrA protein from *E. coli* and Hin47 protein from *Haemophilus* influenzae would be different. In fact, this is true. HtrA from *E. coli* has a different amino acid sequence than that of Hin47 from *Haemophilus influenzae* as shown in Figure 3A and explained on column 5, line 5 through colum 6, line 32 of U.S. Patent No. 5,506,139. This patent is incorporated by reference into the Instant Application as indicated on page 2, lines 15-17 of the Instant Application.

In view of the above, Applicants respectfully submit that the alleged teaching of Bass, as supported by Spiess and Faccio, applies only to chaperone proteins of *E. coli*. The combination of Bass Spiess, Faccio, the 1998 Article and Spaete (or subcombinations thereof) do not teach all of the limitations of claim 5 (and its dependent claims). For the above reasons, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness.

One of skill in the art would not have derived a reasonable expectation of success of using Hin47 as a chaperone protein from the cited references, and that such expectation of success is only found in Applicant's disclosure. As described above, Bass, Spiess and Faccio only relate to *E. coli* chaperones. The 1998 Articles teaches only a non-proteolytic mutant Hin47 and does not teach that Hin47 is a chaperone protein. The addition of Spaete does not add to Bass, Spiess, Faccio or the 1998 Article to provide a basis to establish the reasonable expectation of such of using Hin47 as a chaperone protein. This reasonable expectation of success is found only in the Instant Application. Without such a reasonable expectation of success, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness.

Applicants respectfully further submit that the Examiner has not provided a proper basis for either a suggestion or a motivation to combine the cited references. The Examiner stated that "one of skill in the art would have been so motivated to use hin47 [sic] because it was known as being a chaperone (Bass and the 1998 Article) when its does not lyse the target protein","[t]he 1998 Article teaches that the protease function may be eliminated by mutation.", "one of ordinary skill in the art would have known from the to [sic] references above that Hin47 could have been used in the disclosed vector" of Spaete; and concluded that "...it would have been obvious to one of ordinary skill in the art to use the Hin47 analog in order to avoid the uncertainty involved in

using the active protease." Applicants respectfully submit that the Examiner has not demonstrated that one with skill in the art would have been motivated to combine the teachings of Bass (or Spiess or Faccio), the 1998 Article or Spaete to arrive at the belief that a non-proteolytic Hin47 mutant of the 1998 Article would be useful as a chaperone protein. This is because Bass (or Spiess or Faccio) merely teach that HtrA of *E. coli* is useful as a chaperone protein and the 1998 Article merely teaches that certain Hin47 mutants are non-proteolyic. Nor has the Examiner provided any proper basis for either a suggestion or a motivation to combine Spaete with Bass (or Spiess or Faccio) and the 1998 Article, or any other prior art to demonstrate that one with skill in the art would combine the teaching of Spaete with Bass (or Spiess or Faccio) and the 1998 Article to arrive at the invention of the Instant Application. This is because the Spaete appears to merely teach a method involving the use of compatible escort proteins (such as human FGF receptor and cytomegalovirus UL115) to shuttle recombinant cytomegalovirus glycoproteins (such as CMV gH) co-expressed with the escort proteins to the cell surface, where the co-expression is performed in either mammalian or insect cells. There is no basis in Spate for either a suggestion or motivation to apply its teaching to Bass (or Spiess or Faccio) relating to HtrA of *E. coli* as a chaperone protein or the 1998 Article relating to non-proteolytic Hin47 mutants of *Hameophilus*.

Thus, the Applicants respectfully submit that the Examiner has not made a *prima facie* case of obviousness under 35 U.S.C. 103(a) as to claim 5, 6 and 8 because the Examiner has not been shown that the prior art reference (or references when combined) teach or suggest all the claim limitations, has not shown a reasonable expectation of success if the references are combined, and has not shown that the teaching or suggestion to make the claimed combination and the reasonable expectation of success are both found in the prior art, and not based on applicant's disclosure Accordingly, Applicants respectfully request that the Examiner withdraw this rejection.

3. Rejection of claims 9-11 under 35 U.S.C. 103(a).

Claims 9-11 were rejected in a prior action (Office Action, mailed June 4, 2002) under 35 U.S.C. 103(a) as being unpatentable over Bass (Bass, S. et al., *J. Bacteriology*, 178:1154-61 (1996)), in view of the 1998 Article (Loosmore, S.M. et al., *Infection and Immunity*, 66(3): 899-906 (1998)) and Spate (U.S. Patent No. 5,474,914 issued Richard Spate, 1995), and in further view of Barenkamp (Barenkamp, S.J. et al, Molecular Microbiology, 19(6): 1215-1223 (1996)) and the '182 Patent (U.S. Patent No. 6,335,182 issued to Sheena M. Loosmore et al., 2002).

First, Applicants respectfully submit that the '182 Patent must be disqualified as prior art against the Instant Application. 35 U.S.C. 103(c) provides that "Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person." The 182 Patent cannot be used as not prior art under 35 U.S.C. 103(a), as it is not prior art under 35 U.S.C. 102(b) because it was published January 1, 2002 which is after the May 25, 2000 filing date of the Instant Application. Also, the 182 Patent cannot be used to as prior art under 35 U.S.C. 102(e) because the subject matter of the 182 Patent and the claimed invention of the Instant Application were, at the time the invention was made, owned by the Aventis Pasteur Limited or subject to an obligation of assignment to the Aventis Pasteur Limited. Applicants attach a copy of the first page of the 182 Patent demonstrating that it was assigned by its inventors (Sheena M. Loosmore, Yan Ping Yang and Michael H. Klein) to Aventis Pasteur Limited, and attach the assignment of the invention of the Instant Applicaton by the inventors (Sheena M. Loosmore and Yan Ping Yang) to Aventis Pasteur Limited. The Applicants hereby state that at the time the invention was made they were each subject to an obligation of assignment of the invention to Aventis Pasteur Limited.

Second, the Examiner characterized Barenkamp as teaching that the Hia protein may also be used as a vaccine against *Haemophilus influenzae*. The inclusion of the teaching of Barenkamp with the teachings of Bass, the 1998 Article and Spaete does not assist in the establishment a prima facie case of obviousness under 35 U.S.C. 103(a) because, as discussed above, Bass (or Spiess or Faccio) does not teach that Hin47 would be useful as a chaperone protein. Thus, the Examiner has not made a *prima facie* case of obviousness under 35 U.S.C. 103(a) as to claims 9-11 because it has not been shown that the prior art reference (or references when combined) each or suggest all the claim limitations. Accordingly, Applicants respectfully request that the Examiner withdraw this rejection.

Should the Examiner have any questions concerning this application, he is invited to contact the undersigned at (570) 839-5537. If necessary, please charge any additional fees required or credit any fees overpaid to Deposit Account No. 50-0244.

Respectfully submitted,

Date: May 17, 2004

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